press release

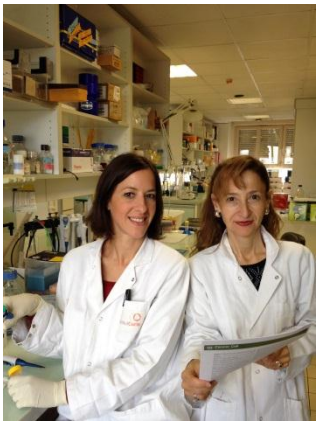
13 October 2015

OVARIAN CANCER

A promising approach for treating the most aggressive forms using targeted therapy.

Thanks to work done at Institute Curie by a team led by Fatima Mechta-Grigoriou, Inserm Research Director, it is now possible to identify, among women with aggressive ovarian cancer, those who could benefit from a promising targeted therapy.

The Stress and Cancer team (an Inserm/Institut Curie team designated by the French National Cancer League), directed by Fatima Mechta-Grigoriou (photo, right), has just taken a major step toward identifying women with an aggressive form of ovarian cancer who are likely to benefit from targeted therapy in the form of a MEK inhibitor.



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Finding the Achilles heel of ovarian tumour cells

"75% of ovarian cancers are high grade, i.e. highly aggressive. The mutation profile differs between low- and high-grade tumours," explains Virginie Mieulet (photo, left), post-doctoral fellow and co-author of this work. *"For example, alterations in the KRAS/BRAF oncogenes are present in 70% of less aggressive tumours, but in only 1% of aggressive tumours."*

Moreover, BRAF activates the MEK signalling pathway[1] involved in the development of low-grade ovarian tumours. MEK inhibitors have therefore been proposed as a possible therapeutic solution for these cancers.

Fatima Mechta-Grigoriou and her team show that prescription of MEK inhibitors could extend to high-grade tumours. Because the MEK pathway is activated in 50% of high-grade ovarian tumours, even in the absence of KRAS/BRAF mutations. Why? *"Because of MAP3K8 accumulation,"* explains the researcher. *"This protein controls tumour progression by regulating the cell cycle and tumour invasion, thus playing a key role in the development of ovarian cancers."*

"The MAP3K8 protein might serve as a biomarker for identifying patients likely to benefit from a therapy based on MEK inhibition," adds Fatima Mechta-Grigoriou,

[1] Because of the key role of the MEK signalling pathway in carcinogenesis—activation is observed in 30% of cancers—MEK inhibitors constitute a promising therapeutic approach. Clinical trials are currently underway for several tumour locations (skin melanoma, intestinal tumours, thyroid cancer, etc.).

Inserm Research Director, "especially since it can be quite simply detected from a tissue section by our physician pathologist colleagues, who, incidentally, have helped us greatly in this work."

While clinical trials are already underway to assess MEK inhibitors in low-grade ovarian cancers, everything seems to point to the interest of developing a clinical trial in women with high-grade ovarian cancer overexpressing *MAP3K8*, to evaluate the efficacy of this targeted therapy, in addition to the conventional chemotherapies.

Reference

MAP3K8/TPL-2/COT is a potential predictive marker for MEK inhibitor treatment in high-grade serous ovarian carcinomas

Tina Gruosso [1,2] , Camille Garnier [1,2], Sophie Abelanet [1,2], Yann Kieffer [1,2], Vincent Lemesre [1,2], Dorine Bellanger [3,2], Ivan Bieche [4], Elisabetta Marangoni [5], Xavier Sastre-Garau [6], Virginie Mieulet [1,2,§] and Fatima Mechta-Grigoriou [1,2,§]

1 Stress and Cancer Laboratory, Institut Curie, 26, rue d'Ulm, 75248 Paris

2 Inserm, U830, Paris, F-75248

3 Genomics and Biology of Hereditary Breast Cancers, Institut Curie, 26, rue d'Ulm, 75248 Paris

4 Department of Pharmacogenomics, Institut Curie, 26, rue d'Ulm, 75248 Paris

5 Laboratory of Preclinical Investigation, Translational Research Department, Institut Curie, 26, rue d'Ulm, 75248 Paris

6 Department of Pathology, Institut Curie, 26, rue d'Ulm, 75248 Paris

§ These authors contributed equally to the work

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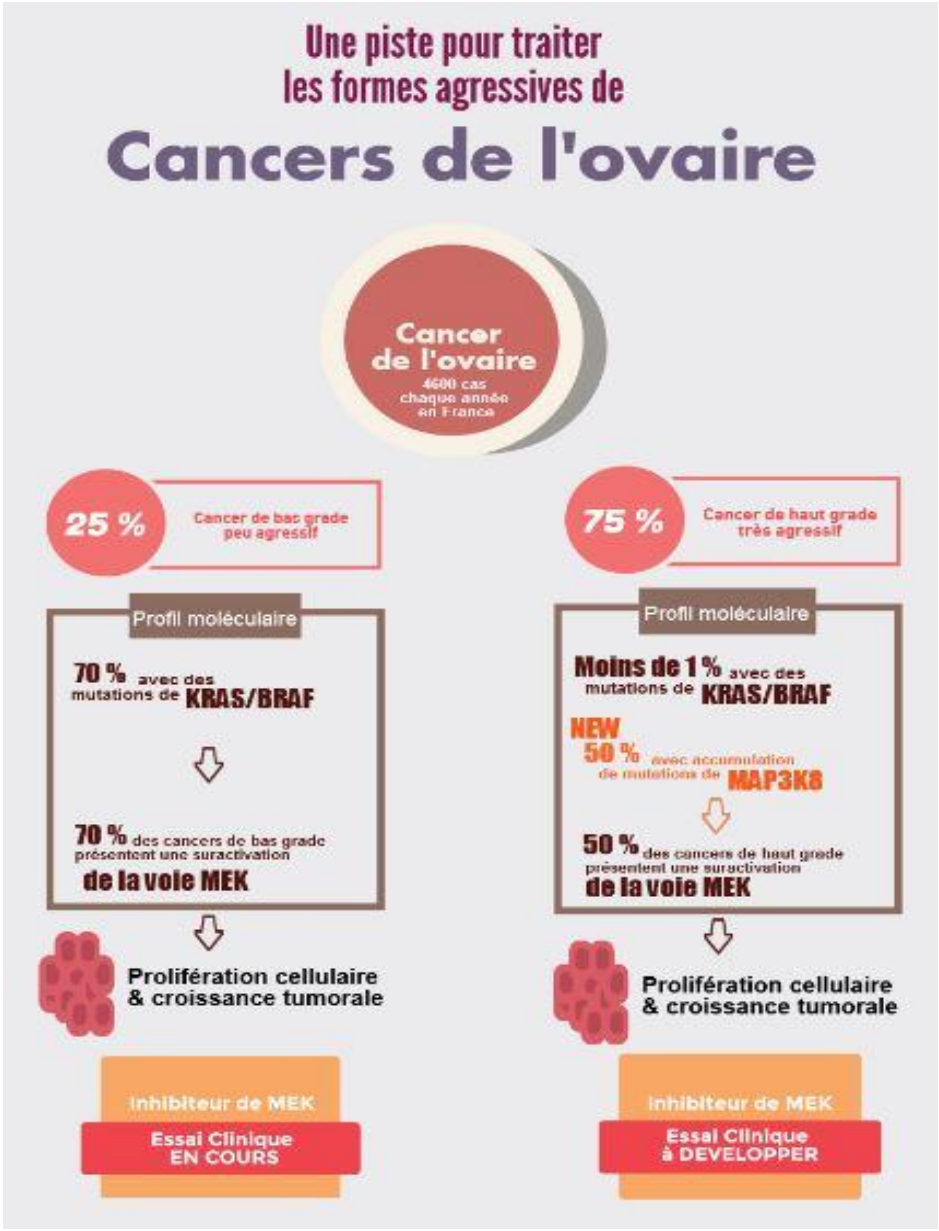
Read the article

http://www.nature.com/ncomms/2015/151012/ncomms9583/full/ncomms9583.html

Ovarian cancer affects nearly 4,600 women in France each year. An ovarian tumour can develop silently for quite a long time, and thus attain a large size before causing symptoms that induce the woman to seek medical advice. This explains why this cancer is often diagnosed at an advanced stage. It is responsible for 3,150 deaths per year. Treatment is based mainly on a combination of surgery and chemotherapy. The choice between the different treatment options depends on the morphology of the tumour cells, their rate of proliferation, disease spread, etc. Analysis of the molecular profile of tumours could soon contribute to this decision and improve management. In most women with ovarian tumours, combination chemotherapies (platinum-taxane chemotherapy) have been shown to be effective. However, once a recurrence is diagnosed, there is no really effective treatment at this time.


Une piste pour traiter
les formes agressives de
Cancers de l'ovaire
Cancer de l'ovaire
4600 cas chaque année en France
25 %
Cancer de bas grade peu agressif
Profil moléculaire
70 % avec des mutations de KRAS/BRAF
70 % des cancers de bas grade présentent une suractivation de la voie MEK
Prolifération cellulaire & croissance tumorale
Inhibiteur de MEK
Essai Clinique EN COURS
75 %
Cancer de haut grade très agressif
Profil moléculaire
Moins de 1 % avec des mutations de KRAS/BRAF
NEW
50 % avec accumulation de mutations de MAP3K8
50 % des cancers de haut grade présentent une suractivation de la voie MEK
Prolifération cellulaire & croissance tumorale
Inhibiteur de MEK
Essai Clinique à DEVELOPPER

An approach for treating aggressive forms of

Ovarian cancer

Ovarian cancer
4,600 cases in France each year

25% Low-grade cancer, not highly aggressive

Molecular profile

70% with KRAS/BRAF mutations

70% of low-grade cancers show overactivation of the MEK pathway

Cell proliferation and tumour growth

MEK inhibitor

Clinical trial UNDERWAY

75% High-grade cancer, highly aggressive

Molecular profile

Fewer than 1% with KRAS/BRAF mutations

NEW
50% with accumulation of mutations in MAP3K8

50% of high-grade cancers show overactivation of the MEK pathway

Cell proliferation and tumour growth

MEK inhibitor

Clinical trial TO BE DEVELOPED

To find out more: Information file, *Cancers de l'ovaire* (Ovarian cancers)

Institut Curie, in brief

Institut Curie, a leading player in action on cancer, combines the leading French cancer research centre with a state-of the art hospital group that is a referral centre for the care of breast cancers, paediatric tumours and eye tumours. Founded in 1909 by Marie Curie, Institut Curie has over 3,400 researchers, physicians and nursing staff involved in its 3 missions, i.e., treatment, research and teaching. A recognised private non-profit foundation, authorised to receive donations and bequests, Institut Curie can, with the support of its donors, spur discoveries and thereby improve patient treatment and quality of life. To find out more: **www.curie.fr**

PRESS CONTACT Catherine Goupillon-Senghor – +33 (0)1 56 24 55 23 - 06 13 91 63 63

service.presse@curie.fr

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Together, let's beat cancer